Prevalence and characteristics of gallstone disease in an Iranian population: a study on cadavers

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BACKGROUND: **The prevalence of gallstones is low in Asians. In Iran, many factors influence the prevalence of this disease. The aim of this study was to determine the prevalence of gallbladder stones and their chemical characteristics in a population by the study of cadavers.**

METHODS: **In this cross-sectional study, autopsies were performed on 253 cadavers of more than 13 years old. The cadavers were studied to determine the number, location of stone formation, chemical composition, dry weight, and mean diameter of stones in the gallbladder and common bile duct.**

RESULTS: **The prevalence of gallstone disease in these cadavers was 6.3% (men 4.7%, women 8.6%, not significantly different, P=0.216). There was a positive relationship between the age and prevalence of gallstone disease (P=0.033). The most common stone compositions were cholesterol and oxalate. The mean diameter (P=0.0058) and dry weight (P<0.0001) of stones were higher in the gallbladder than in the common bile duct. Positive relations between the amount of oxalate and mean diameter, and between the amount of oxalate and mean dry weight of gallstones were found, but the relationship between the amount of cholesterol and mean diameter was inverse.**

CONCLUSIONS: **The prevalence of gallstones differed among age groups. Diameter and dry weight of gallstones were dependent on location of stone formation and chemical composition.**

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KEY WORDS: **gallstone; gallbladder; common bile duct; prevalence; cadavers**

Introduction

Gallbladder disease is one of the most common gastrointestinal disorders worldwide.[1] Many studies to identify risk factors for biliary lithiasis in the west have focused on hypersaturation of cholesterol in bile in the nucleation process, a critical step in the genesis of bile stones.[2, 3] A high concentration of cholesterol has been found in as much as 80% of stones in patients of Western countries.[4]

Every year, 1%-3% of people worldwide develop gallstones and about 1%-3% of them are symptomatic; the morbidity and fatality are associated with symptomatic cholelithiasis, cholecystitis, or cholangitis.[5] Unfortunately, gallbladder stone composition is heterogeneous, and differs within and between populations around the world.[6, 7] In Iran, gender and age are important factors in the prevalence of gallstone disease. The prevalence in men and women, aged 31-40 years, is very low. It is sharply increased by more than 10-fold in men older than 60 years and women older than 50 years.[8] Over half of the patients are asymptomatic, and usually detected by abdominal ultrasonography.[9] Today, the prevalence of gallstone disease has increased considerably with the wide use of ultrasonography.[10]

There are few reports on the prevalence of gallstone disease in Asia and, to date, few data on its frequency have been published in Iran. The increasing frequency of biliary stones in Iran, with its different epidemiological factors and diseases, has prompted us to determine the prevalence of gallbladder stones and

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their chemical characteristics in this population by the study of cadavers.

Methods

This study was approved by the Ethics Committee of Tehran Legal Medicine Center and Medical Sciences/ Tehran University. We examined the gallbladder and common bile duct (CBD) in 253 cadavers selected randomly from 5400 referred to the Tehran University Tissue Archive over a period of 9 months. In this cross-sectional study, autopsies were performed in the 253 cadavers of more than 13 years old. The most common causes of death in these cases were accident, suicide, and sudden death.

After opening the mid-anterior chest and abdomen, the gallbladder was located, cut, and examined for the presence of stones in the gallbladder and CBD. Then, the number, dry weight (by digital balance), and mean diameter of stones (by Collis) were determined. Stones were transferred to the laboratory for determination of their components (with a special kit for gallstone analysis).

The results were expressed as the mean±standard deviation (SD) for quantitative variables and percentage for categorical variables. Categorical variables were compared using the Chi-square test, Fisher's exact test and two-tailed Student's *t* test to compare two means, and Spearman's rank-order correlation coefficient for nonparametric correlations. *P* values of 0.05 or less were considered statistically significant. All statistical analyses were performed using SPSS version 13.0 and SAS version 9.1 for Windows.

Results

Among cadavers with gallstone disease, 58.5% were male. The prevalence was 6.3% (men 4.7%, women 8.6%; statistically similar, $P=0.216$). No gallstone was found in cadavers younger than 35 years, but it was frequently found in those aged 56 to 65 years (Fig.). There was a positive correlation between age and prevalence of gallstone disease ($P=0.033$).

The gallstones were single in 37.5% of cases, double in 18.8%, triple in 25% and 4 stones were found in the rest. Four CBD stones were found in each of two cadavers.

The type and chemical composition of stones in the gallbladder and CBD are shown in Table 1. The most common compositions were cholesterol and oxalate, both in gallstones and CBD stones.

The mean diameter of stones was higher in the gallbladder than in the CBD (12.60±6.07 vs. 5.20±1.55 mm, $P<0.0001$). The mean dry weight was also higher in gallbladder (2.69±0.91 vs. 1.07±0.21 mg, $P<0.0001$).

There was also a positive correlation between the amount of oxalate and mean diameter of gallstones, but the correlation between the amount of cholesterol and mean diameter was inverse. No significant

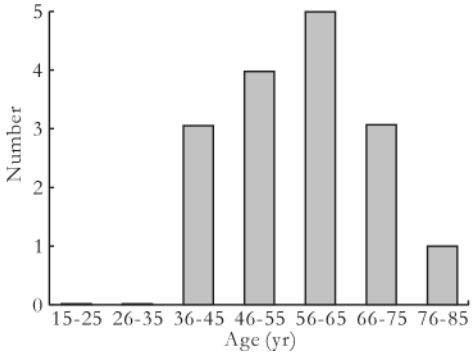

Fig. Age distribution of cadavers with gallstones.

Table 1. Chemical composition of stones in the gallbladder and CBD (%)

Chemical composition of stone	Gallbladder (n=36)	CBD (n=8)	*P* value
Cholesterol	50.46	50.28	0.991
Oxalate	23.11	23.73	0.971
Biliary salts	10.25	10.97	0.953
Urate	3.88	4.08	0.978
Cystein	0.49	0.45	0.979
Magnesium-ammonium-phosphate	0.42	0.39	0.988
Phosphate	0.37	0.40	0.990
Others	10.94	9.66	0.376

Table 2. Relation between stone composition and mean diameter and dry weight of gallstones

Chemical composition of stone	Mean diameter of gallstone		Mean dry weight of gallstone	
	Spearman coefficient	*P* value	Spearman coefficient	*P* value
Cholesterol	-0.50	0.040	-0.42	NS
Oxalate	0.53	0.030	0.55	0.020
Biliary salts	-0.17	NS	-0.07	NS
Urate	-0.11	NS	-0.16	NS
Cystein	-0.30	NS	-0.23	NS
Magnesium-ammonium-phosphate	0.24	NS	0.27	NS
Phosphate	-0.12	NS	-0.02	NS

NS: not significant.

correlation between the amount of other components and diameter was found (Table 2). Also, the amount of oxalate and mean dry weight were positively correlated, but there was no correlation between the amount of other components and dry weight (Table 2).

Discussion

The number of gallstone cases has gradually increased.[11] Ten to fifteen percent of caucasian adults in developed countries harbour gallstones.[12] It has been suggested that gallstone disease is now more common, and that this might explain an increase in cholecystectomy rates, although conclusive evidence is lacking. Gallstone disease was much more common in 1974-1998 than in 1953-1973.[13] In Iran, gallstone disease is very uncommon in the middle-aged, but increases sharply in older people. However, this does not reach the high prevalence seen in Western countries.[8]

Certain risk factors for gallstones are immutable: female gender, increasing age and ethnicity/family (genetic traits). Others are modifiable: obesity, the metabolic syndrome, rapid weight loss, certain diseases (cirrhosis, Crohn's disease) and gallbladder stasis (from spinal cord injury or drugs like somatostatin). The only established dietary risk is a high caloric intake.[12] In Iran, the intake of a high fiber diet, and low numbers of people who are overweight, have a smoking habit and hyperlipidemia are probably the reasons for this low prevalence.[8]

In this study, we found that although the prevalence of gallstone disease was numerically higher in females than males (8.6% vs. 4.7%), there was no statistical difference. Also, gallstone disease was frequently found in cadavers more than 56 years old. In the study by Zhu et al, the disease occurred mostly in females over 50, with a female-male incidence of 2.57% vs. 1.80%.[14] We found no gallstone disease in patients aged less than 35 years. In a similar study in Iran, the prevalence in men and women in the age group of 31-40 years was very low (0.3% in men and 1.8% in women), but it increased sharply by more than 10-fold in men older than 60 years and women over 50 years (12.5% and 24.6% in males and females aged 71-80 years, respectively).[8] In the study by Bateson et al,[13] increasing age was also the main determinant of gallstone disease. Though it was more common in women than men aged 40-89 years, there was no sex difference under 40 or over 90 years. Gallstones were definitely more common in both sexes at all ages over 40 in the last 25 years.[13] However, the age and sex distribution of gallstones may be related to the location of stone formation. In Park's study, a female predominance was not found (F/M=1.17-1.37) and the patients with CBD stones were older than those with gallbladder stones.[11]

In our study, the most common stone compositions in the gallbladder and CBD were cholesterol and oxalate. Epidemiology, pathogenesis and classification of stones are very likely to differ according to their location.[15] Furthermore, gallbladder stones are primarily cholesterol. More than 90% of all cholesterol and black stones are found in the gallbladder. Different types of gallstones show a tendency to occur in certain regions; however, they may be formed in almost any part of the biliary system if conditions are favorable.[16] When stones are present in both the CBD and gallbladder, the duct stones are similar in chemical composition to gallbladder stones in the majority of cases and are predominantly cholesterol-type. However, CBD stones from patients whose gallbladders had been removed at least one year before the detection of duct stones contained less cholesterol and more bilirubin than duct stones associated with gallbladder stones.[17]

The gallbladder versus bile duct stone ratio in our study was 8:1. The chemical composition and location of stone formation differs in different populations, such that in developed countries, cholesterol gallstones predominate[12] and the gallbladder versus bile duct stone ratio in these countries is 7.36∶1.[14] Bile duct stones can also be formed in the absence of gallbladder stones, and such primary bile duct stones are more common in East Asian countries than in the Western countries.[15]

We also found that the diameter and dry weight of stones were related to the location of stone formation. In previous studies, an association between composition and location of stone formation was noted.[14, 17, 18] However, the relationship between chemical composition and diameter and weight of stone deserves further study.

In conclusion, the prevalence of gallstone disease in Iran is low and dependent on increasing age; however it is statistically similar between the genders. The chemical composition of gallstones is frequently cholesterol and oxalate. There is an association of diameter and dry weight of stones with location of stone formation.

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